

## (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
25 September 2003 (25.09.2003)

PCT

(10) International Publication Number  
**WO 2003/077859 A3**

- (51) International Patent Classification<sup>7</sup>: **A61K 39/21**
- (21) International Application Number:  
PCT/US2003/007727
- (22) International Filing Date: 12 March 2003 (12.03.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/363,807 13 March 2002 (13.03.2002) US
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- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
- with international search report
  - before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report:  
26 August 2004
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: METHOD OF INDUCING AN ENHANCED IMMUNE RESPONSE AGAINST HIV

(57) Abstract: An efficient means of inducing an immune response against human immunodeficiency virus (HIV) utilizing specific prime-boost regimes is disclosed. The specific prime-boost regimes employ a heterologous prime-boost protocol employing recombinant adenoviral vectors of alternative and distinct serotypes comprising exogenous genetic material encoding a common HIV antigen. Vaccines administered into living vertebrate tissue in accordance with the disclosed regimes, preferably a mammalian host, such as a human or a non-human mammal of commercial or domestic veterinary importance, express the HIV-1 antigen (e.g., Gag), inducing a cellular immune response which specifically recognizes HIV-1. It is believed that the disclosed prime/boost regime will offer a prophylactic advantage to previously uninfected individuals and/or provide a therapeutic effect by reducing viral load levels within an infected individual, thus prolonging the asymptomatic phase of HIV-1 infection.

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/07727

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : A61K 39/21

US CL : 424/199.1, 204.1, 208.1; 435/235.1, 320.1

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/199.1, 204.1, 208.1; 435/235.1, 320.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Continuation Sheet**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	MORRAL et al., Administration of helper-dependent adenoviral vectors and sequential delivery of different vector serotype for long-term liver-directed gene transfer in baboons. Proceedings of the National Academy of Sciences, U.S.A. 1999 Vol. 96 pages 12816-12821, see page 12816, column 2, lines 10-11, Tables 1 and 2, and page 12819, column 1, lines 5- 27.	15, 17- 25, 27- 30
Y	SHIVER et al., Replication-incompetent adenoviral vaccine vector elicits effective anti-immunodeficiency-virus immunity. Nature. 2002 Vol. 415, pages 331-335, see Table 1, and page 335, column 1.	1- 30
A	YOSHIDA T. et al., Activation of HIV-1-specific immune responses to an HIV-1 vaccine constructed from a replication-defective adenovirus vector using various combinations of immunization protocols. Clinical & Experimental Immunology June 2001 Volume 124 Issue 3 Page 445 - 452.	
Y,P	PATTERSON et al., Potent, persistent cellular immune responses elicited by sequential immunization of rhesus macaques with Ad5 host range mutant recombinants encoding SIV Rev and SIV Nef. DNA Cell Biol. 2002 Sep;21(9):627-35, see	1- 3,5- 15, 17- 25, 27- 30



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"I" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

14 September 2003 (14.09.2003)

Date of mailing of the international search report

17 JUN 2004

Name and mailing address of the ISA/US

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# INTERNATIONAL SEARCH REPORT

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## C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	HUANG Y et al., Human Immunodeficiency Virus Type 1-Specific Immunity after Genetic Immunization Is Enhanced by Modification of Gag and Pol Expression. Journal of Virology 2001 Vol. 75, pages 4947-4951, see Figure 3 and page 4950, column 1, lines 1-3.	4,16,26

**INTERNATIONAL SEARCH REPORT**

PCT/US99/07727

**Continuation of B. FIELDS SEARCHED Item 3:**

**WEST, MEDLINE**

adenovirus, HIV, vaccine, boost, optimized, nef, pol, gag, vector